INFANTILE LEISHMANIASIS (MARDA TAL BICCIA) IN MALTA

BY

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There exists in these Islands a morbid condition characterised by great enlargement of the spleen and profound anaemia. It is met with almost exclusively in very young children, and is nearly always fatal.

Although, with the exception of splenic leukaemia, all the anaemias with chronic swelling of the spleen are clinically little differentiated, there always has been a feeling among local practitioners that they were dealing with a special pathological entity, which being in its clinical manifestations very much like some of the better known disorders of the blood and haematopoietic organs, they could not very well, in the absence of some special element of diagnosis, dissociate from the latter.

Etiologically its connection with syphilis, tubercle, rickets, or amyloid degeneration is not apparent; as to malaria, it is not endemic in these Islands. The disease is variously certified at death as leucocythaemia, splenic leukaemia, splenic anaemia, pseudo-leukaemia, splenitis, splenopathy; but in the Maltese language it is referred to by the professional and the layman alike under one name, 'Marda tal biccia.'

The disease begins very insidiously with spells of fever of a slow type, at a period of the child's life when slight ailments are very frequent and not made much of. If the initial pyrexia tends to establish itself without any obvious explanation such as dentition or gastro-intestinal troubles, Mediterranean fever is apt to be suspected, especially as on percussion the spleen is already found somewhat enlarged. More often, the initial attacks of fever do not attract attention until there arrives a time when the child, having lost its

usual brightness and desire for food, becomes pale and begins to lose flesh. By this time the spleen can be felt as a distinct tumour in the left hypochondrium, and the little patient is shown to a doctor. From this stage the malady has a protracted course of from six to eighteen or twenty months.

The following is a short clinical picture of the disease when fully developed:—The skin is waxy white or sallow, according as the subject is fair or dark; the lips and mucous membranes are blanched; the eyes are full of sadness and look abnormally large in the emaciated little face; all the muscles are flabby and more or less atrophic, the distended abdomen contrasting with the wasted thorax, its fulness more pronounced on the left. The outlines of the splenic tumour may sometimes be easily made out by inspection. On examination the spleen is found generally to extend down to the level of the umbilicus, firm but not hard, freely movable, only slightly tender on pressure or not at all, its margins rounded but well defined, its notches well pronounced. In growing downwards as a rule it keeps to the left of the navel, reaching very often down to the iliac crest; but in some cases it fills the pelvis, and, crossing the *linea alba*, occupies the right inferior quadrant, where in an extreme case I have found it in close apposition to the anterior border of the enlarged liver. The occurrence of the *caput medusae* is very common. The liver is also enlarged, but to a less degree, not more than one or two fingers' breadth below the costal margin. In the cases observed the presence of fluid in the abdominal cavity could not be detected. The lymphatic glands accessible to examination are not sensibly enlarged, but when the wasting is very pronounced they can easily be felt and seen. Transitory oedema of the feet, hands and eyelids is common. The appetite is very indifferent, but sometimes there is a great craving for food; it is rarely perverted: in some cases the patients pick and chew bits of plaster or little stones. Gastro-intestinal troubles are the rule, manifested by intercurrent attacks of very fetid diarrhoea. A symptom met with sooner or later consists of a solitary or repeated attack of dysenteriform diarrhoea with tenesmi, slimy motions containing blood and mucus or mucus only. The frequent passage of loose stools is not infrequently accompanied by temporary shrinking of the spleen. In one case this was observed to such a

degree and the improvement of the other symptoms was so marked and continued that the mother firmly believed the abdominal tumour—the spleen—had been passed with the motions. Curiously enough the case ended in complete recovery; the patient, a boy of six, when seen by me was in perfect health. Evidently, he also had had cancrum oris, as the upper middle incisors were missing and the gums were badly scarred. Intercurrent attacks of bronchitis are by no means rare. Epistaxis is a common occurrence, so is bleeding of the gums, and the appearance of one or more crops of purpura all over the trunk and face. In one case a few vibices were observed. A frequent terminal complication is cancrum oris. The mortification may assume formidable proportions in a few days, or it may evolve less acutely, death supervening in a month or six weeks. It sets in very stealthily, almost without pain, the increased flow of saliva at first being ascribed to irritation of the mouth due to dental evolution. The process in the cases observed started from the gums in connection with the upper incisors, lower or upper premolars. The gangrene is often very extensive and exceedingly repulsive to the eye and nose, and the deformity is generally such that no plastic operation could ever remedy. The blood in advanced cases is quite watery; it separates quickly into clot and plasma. Prognosis is very bad. Nearly all practitioners, however, quote from experience one or two instances of the disease ending in recovery; but some maintain that all recoveries are cases of mistaken diagnosis. It is wonderful how some patients can go on living; on the other hand death occurs when least expected. Bronchial complications are very frequent towards the end.

The disease, as outlined, was found to have reached a more or less advanced stage in the twenty-one cases, to which the following notes refer:—

1. Girl, 4 years, seen in May, 1909. Ill since October, 1908, after whooping cough. Intercurrent waves of fever of a remittent type, profuse perspiration, no appetite, anaemia, muscular atrophy, transitory oedema of both legs, spleen reaches down to iliac crest, liver also enlarged, purpura, dysenteric diarrhoea with great loss of blood, bleeding from gums, noma, fall of upper incisors. Peripheral blood examined: two Leishman-Donovan bodies in a large mononuclear, well-marked large mononuclear increase. Died about one month after. No post mortem or puncture of spleen after death allowed.

2. Girl, 4½ years, seen in July, 1909. Very scanty notes taken at the time. Died in January, 1910, after an illness of about fourteen months. Two weeks before death a swelling of the left cheek and a very foul condition of the mouth foreboded

the very common final complication, noma. The disease had started with spells of fever with very high temperature of a remittent type, then anaemia, great pallor of the integuments, enlargement of the spleen, intermittent attacks of diarrhoea, oedema of the extremities followed. Liver moderately enlarged, lymphatic glands not affected. No other cases in the same family. No dogs kept. Smears and sections from spleen post mortem : smears were literally studded with Leishman-Donovan bodies, but the parasites were not so abundant in the sections.

3. Girl, $3\frac{1}{2}$ years, seen in October, 1909. Had measles in April, 1908. About four months ago had fever for twenty days, no high temperatures, no regular type. She gradually became anaemic and lost flesh. Now her skin is of an earthy pallor, marked muscular atrophy, no oedema, no haemorrhages, the appetite very poor, is at times abnormal, has diarrhoea every now and then, no blood with stools. Spleen is enlarged down to two fingers' breadth below the navel. Anterior border of liver is two fingers' breadth below costal border on mammillary line Glands not enlarged. No noma. Died about three months after.

4. Boy, 25 months, seen in October, 1909. Ill since six months. Mother did not notice any fever at first; two months after he had a spell of dysenteric diarrhoea with loss of blood. Now he is very pale and has lost flesh, very fretful, glands not enlarged, no oedema, fever of an irregular type. Spleen reaches down to three fingers' breadth below navel, no marked increase of liver. Mother stated that she had had the same disease when a child. Case has not been seen again.

5. Boy, 6 years, born in Malta of English parents, seen in October, 1909. Ill since one year. Spleen began to increase in size about five months ago. Extreme anaemia and wasting, spleen enormous, spells of fever every now and then, appetite good, no purpura, no bleeding from gums, no blood with stools, one or two vibices on the back. Later on had several purpuric eruptions, bleeding from gums, profuse diarrhoea. The doctor attending noticed an almost complete retraction of the spleen a few days before the end and the diarrhoea ceased, but there was no amelioration of the other symptoms. The child died of exhaustion in April, 1910.

6. Girl, 3 years, seen in November, 1909. Ill since one year. Moderate anaemia, no marked wasting, no oedema, has a temperature every now and then, appetite good. Spleen reaches to just below navel. Has had purpura and dysenteric attacks but no bronchial phenomena. Glands not enlarged. Blood smears from ear : no parasites. Child lost sight of. Doctor attending stated to have observed a great improvement following a course of injections of methyl arsenate of iron.

7. Girl, 6 years, seen in December, 1909. Ill since one year, after sustaining a fractured clavicle. Earthy colour, extremely anaemic; very extensive gangrene of gums, both lips, nose and cheeks. Great emaciation. Spleen, but for the enlarged liver which reaches to about four fingers' breadth below costal margin, occupies the whole abdomen; has dysenteric diarrhoea; appetite fairly good. Died four days after. No examination of the blood or spleen puncture allowed. A sister died from the same disease when two years old : had noma followed by same extensive gangrene. An elder brother, who is stated also to have had the disease when six years old, is now quite well. An aunt and a cousin on the mother's side are supposed to have died of the same complaint.

8. Boy, 3 years, seen in January, 1910. Ill since eighteen months, spells of fever with profuse perspiration, intercurrent attacks of diarrhoea and bronchitis, purpura, epistaxis, bleeding from gums, extreme pallor and emaciation. Face has a very old and sad look. The spleen free, firm, notchy, easily movable, not painful, reaches down to the inguinal fold; liver has grown to four fingers' breadth below the costal margin. Died suddenly in February. Two dogs had been in the house for a long time. A fragment of spleen obtained post mortem : Leishman-Donovan bodies in smears and sections.

9. Girl, 5 years, seen in January, 1910. Ill since November, 1909. Had whooping cough a year ago. The disease began with spells of fever and anaemia, then swelling of the spleen; this organ now reaches to inguinal fold; liver is little enlarged. She is very pale and very sad, has diarrhoea, no blood with stools, no epistaxis, no bleeding from gums, no purpura, feet are oedematous. A cousin on mother's side died from the same complaint when eighteen months old. Seen again in April, no change; administration of *Tr. senegae* suggested. Seen again in October: very marked improvement, the spleen has receded to one finger's breadth below the costal margin, the child has recovered her gaiety, has a healthy colour and good appetite. One dog in house.

10. Boy, 3½ years, seen in January, 1910. Ill since seven months, after a fright, as stated. Spells of fever, loss of appetite, great pallor and emaciation, oedema of feet, hands and eyelids, great sadness, dysenteric diarrhoea and bronchial catarrh. The splenic tumour fills the left inferior and part of the right inferior quadrant; the liver reaches down to a finger's breadth below costal margin. Seen again in February, the spleen maintains the same curved configuration but does not reach quite down to the ilium, the liver is also smaller, the diarrhoea persists, general condition worse. Peripheral blood examined, no parasites. Died in November, 1910. A brother died of the same disease in June, 1907, when two years old, after an illness of fourteen months. No dogs.

11. Boy, 3 years. He is one of six, of which the eldest is 14 years old and the youngest 15 months. No other children have had the disease. Ill since fifteen months. It was only after three months of irregular fever that the enlarged spleen began to attract attention. Iron preparations were prescribed. After three months' treatment the splenic tumour was so reduced in size that the mother believed him cured. He then contracted whooping-cough and the spleen started growing again. About the time this patient sickened two other children living near were suffering from splenic anaemia, both developed cancrum oris and died. A dog was owned by these people. I saw the child in March, 1910, three days before death: great pallor and emaciation, oedema of feet and eyelids, spleen reaches down to one finger's breadth from iliac crest, liver moderately enlarged, diarrhoea, a black stool occasionally (melaena?). Cancrum oris started opposite right upper premolars, now mortification of right cheek, exposure of buccal cavity; no epistaxis, no purpura. Post mortem: Cancrum oris, extensive destruction of right cheek and gums, loss of teeth. Lungs: right, caseous lobular pneumonia; left, emphysema. Heart: all cavities dilated. Liver: enlarged, consistency increased. Spleen: weight 8½ ounces, about three times normal size, rounded margins, many notches, very firm, capsule thickened and adherent; the cut surface greyish towards the middle, brownish-red at periphery, malpighian corpuscles prominent. Mesenteric glands enlarged, not caseous, the other glands normal in size and appearance, bone marrow body of femur reddish and swollen. Smears and sections of spleen and liver show a fair number of Leishman Donovan bodies. Smears from mesenteric glands, a few parasites present. Smears from bone marrow, owing to defective fixation, could not be stained successfully.

12. Girl, 4 years, seen in March, 1910. Has had fever and diarrhoea since three months, moderate emaciation, skin and mucous membranes anaemic, loss of appetite, the child is listless and sad. Diarrhoea every now and then, with tenesmi and passage of mucus, but no blood. Splenic tumour rather narrow, it does not reach below navel, easily movable, not painful; liver cannot be felt on palpation, lymphatic glands normal in size. Seen again in December. Abdomen greatly distended as the splenic tumour has grown down to the iliac crest and, to the right, under the linea alba, the liver is two and a half fingers' breadth below the costal margin, cervical glands are larger than normal, eyelids are oedematous, respiration is much hindered, hollow cough, fever, no haemorrhages.

December 3rd, 1910.—Peripheral blood examined: no parasites. Relative leucocytic values: Large mononuclear, 36·2; small mononuclear, 29·4; transitional, 7·0; polynuclear, 26·2; eosinophile, 1·2.

13. Girl, 3 years. One of a large family, but no other member ever had the disease. A child next door died of splenic anaemia in 1902. Patient has been ill since December, 1909. In January, 1910, had a slight attack of diarrhoea with tenesmi; after three or four weeks of fever, attended with profuse perspiration, mother noticed the splenic tumour just below costal margin. Seen by me in March: no marked emaciation, moderate anaemia, no oedema, no purpura, appetite fair, no great depression. Splenic tumour reaches down to three fingers' breadth below costal margin, liver is just palpable, no diarrhoea. Splenic puncture with an ordinary hypodermic needle, usual antiseptic precautions: Leishman-Donovan bodies present in a fairly large number. Treatment with senega preparations suggested. Marked improvement during the next two months; the case, however, ended fatally in September.

14. Boy, 21 months. Ill since August, 1909. Two cousins on mother's side of about the same age died from same disease after a year's illness. In August, 1909, after a fright, the boy started having a temperature at irregular intervals, with perspiration; several attacks of dysenteric diarrhoea, slight epistaxis and crops of purpura followed. Seen in March, 1910: great pallor of skin and mucous membranes, loss of flesh, profuse salivation, initial mortification of gums at the base of left premolars and slight bleeding, oedema of feet and eyelids. Spleen enlarged down to iliac crest, moderately hard, freely movable, not painful, very marked notches, liver just palpable. Died in April.

15. Boy, 19 months, seen in March, 1910. No history of splenic anaemia in the family—a large one. Ill since $4\frac{1}{2}$ months; spells of fever with perspiration. No diarrhoea, no bronchial catarrh, no epistaxis. Appetite good but perverted, is always picking and chewing stones. On examination: moderate anaemia, no great loss of flesh, gums normal, splenic tumour reaches down to iliac crest and to the right, $1\frac{1}{2}$ inches beyond linea alba, liver can be felt two fingers' breadth below costal border. Splenic puncture: Leishman-Donovan bodies present in all smears in moderate numbers. Treatment: tinctura senegae in large doses. Seen again in April: extreme pallor, slight bleeding from gums, purpura. Died the same month.

16. Boy, 18 months, seen in April, 1910. There is a history of short spells of fever before mother noticed that spleen was enlarged, five months ago. Since then has had diarrhoea off and on, slight bleeding from gums, a few spots of purpura, no oedema. Now skin and mucous membranes anaemic, loss of flesh, appetite fairly good, spleen reaches down to iliac crest and laterally almost to umbilicus, caput medusae, liver one finger's breadth below costal margin, lymphatic glands not enlarged. Splenic puncture: no parasites met with. Died in August.

17. Boy, 2 years. Weakly child from birth. Seen in April. About two months before had enteritis with tenesmi, passage of mucus but no blood, no haemorrhages. Cancrum oris started three weeks before I saw him, when a small slough formed in the gums over the upper incisors. Mother never noticed any enlargement of spleen. Now great pallor and emaciation, diarrhoea, prolapsus ani, mortification of upper lips, nose, cheeks and lower eyelids. Spleen and liver can hardly be felt on palpation, but abdomen is very distended. Died 20th April, 1910. Post mortem, partial: spleen exceeds costal border by about two fingers' breadth. Spleen smears swarming with Leishman-Donovan bodies. About a year ago they had a small dog in the house. Eldest sister died five years ago; two other boys and a baby, of whom the former are older than patient, all alive. Eldest sister was ill for one year, and presented the following symptoms: progressive anaemia and emaciation, fever, attacks of diarrhoea with passage of mucus and prolapsus ani, but no enlargement of spleen was noticed by mother. Then gums in connection with lower left molars underwent a process of mortification which extended to cheek, sloughing through. At that time they also kept a dog different from one mentioned above.

18. Girl, $2\frac{1}{2}$ years. Seen in May, 1910. Ill since five months: Anaemia, emaciation, loss of appetite, diarrhoea with passage of mucus and tenesmi. Now great dejection, bronchitis, no oedema, splenic tumour reaches to about four fingers' breadth below costal margin, liver enlarged but to a less extent, lymphatic glands normal. Died August, 1910.

19. Boy, 15 months. Not seen during life. Post mortem, twenty-four hours after death, 2nd June, 1910: extreme anaemia, mucous membranes bleached, no great emaciation, spots of purpura, oedema of lower limbs, liver very large especially left lobe, splenic tumour reaches to about two fingers' breadth from iliac crest, and is pushed to the left by the enlarged liver, cancrum oris with loss of upper incisors, mortification of gums, upper lip, left cheek, and nose up to lower eyelids on both sides, lymphatic glands normal. Spleen: 5 inches by 3 inches, weight 6 ounces, perisplenitis, patches of infarction, free edges rounded, deep notches, firm but not hard. Liver: 7 inches by $4\frac{1}{2}$ inches, weight $14\frac{1}{4}$ ounces, uniform yellowish white colour, on section very anaemic, dry, mottled appearance. Abdominal cavity contains a small amount of clear yellowish fluid. Mesenteric glands colourless, normal size. Lungs very anaemic, otherwise normal. Heart flaccid and anaemic, pericardium contains a moderate quantity of clear transparent fluid. Smears and sections from spleen, liver and kidneys contain Leishman-Donovan bodies, numerous in the spleen, very few in the kidneys.

20. Girl, 2 years. Ill since April, 1910. At first fever of slow type lasting two weeks. In September the child, who had acquired a sickly hue and lost flesh, started again having a temperature, and by the middle of November the spleen was so enlarged as to be easily palpable. Had no diarrhoea, appetite maintained, no petechiae, no epistaxis, slight bleeding from gums, no oedema. She is the fifth child in a family of six, all in good health; but a cousin on the mother's side died of the disease. No dogs kept. Seen on the 25th of November: very pale and emaciated, no oedema, no purpura, has a hollow cough. Spleen comes down to the level of navel, liver is not palpable. Abscess the size of a large walnut just behind angle of right mandible, gums normal, diarrhoea with tenesmi and passage of blood-tinged mucus. Spleen puncture: Leishman-Donovan bodies in large amount, mostly free, some in large mononuclears, others in groups of 8 to 11.

21. Girl, $2\frac{1}{2}$ years. Ill since three months (?). Seen in December, 1910. Great anaemia and emaciation, rise of temperature at irregular intervals, diarrhoea with tenesmi but no blood, cancrum oris starting over first left upper premolar, cheeks swollen hard and tender, has had no haemorrhages, no oedema, accessible lymphatic glands normal, appetite maintained. Spleen freely movable and painless, occupies upper and lower left quadrant, the liver reaches down two and a half fingers' breadth below costal margin. P. is the youngest of five, of which two died when quite small, eldest two are living and in good health. A dog kept up to ten months ago. Splenic punctures: Leishman-Donovan bodies present in fairly large numbers.

For the observation of these cases I am indebted to the kindness of medical colleagues practising in different parts of the Island, especially Dr. Cannataci, Dr. Wirth, and the staff of the Central Hospital. The symptomatology, the age of the patients, the almost constantly fatal termination, all point to a common morbid condition. It is likewise justifiable to infer that the majority of deaths catalogued under the different names referred to before, more especially if belonging to a certain age period, are instances of one and the same disease.

The question now arises whether all the deaths due to this disease are caused by *Leishmania* infection. Up to the time of writing* *Leishmania infantum* has been found in nine out of ten cases by examination of the spleen and other organs, and in one out of three cases in which films of peripheral blood were stained. These facts do not as yet justify generalisation, the more so as no case of infantile leishmaniasis should be counted as such unless the clinical diagnosis be supported by the demonstration of the specific protozoa; but they go very far to show that the bulk of deaths under five certified as due to leucocythaemia, splenic leukaemia, pseudo-leukaemia and splenitis are cases of *anaemia infantum a leishmania* (G. Pianese, 1905), or *infantile kala-azar* (C. Nicolle, 1908).

The conditions I have found associated with the disease will now be reviewed. The disease is not notifiable, hence all considerations regarding its incidence are based on the deaths imputable to it. Having regard to its fatality, the deaths must fall very little short of the number of attacks.

Locality. During the ten years, 1899-1908, 686 deaths under five were registered in Malta and 58 in Gozo. In order to form an idea of the prevalence of the disease in the various localities the population under five for Malta and Gozo and for the different populated centres in Malta, as estimated in the last census, 1901, have been divided into the number of deaths for the said decennium and the results multiplied by 100. The figures obtained may be taken to represent a sort of endemic index expressing with some degree of approximation the intensity of the disease in the different

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* The following are some notes kindly given me by Captain W. L. Baker, R.A.M.C., of a case under his care :—

Male child, aged 19 months. First seen end of June, 1910. Spleen then enlarged to umbilicus.

Blood Count ... R.C. 4,000,000 per c.cm.
W.C. 4,400 ,,
Hgb. Index 25 per cent.

Spleen became more enlarged and child developed diarrhoea with passage of blood, small haemorrhages also occurred in skin of limbs and trunk. Anaemia increased, and in the middle of August the count was :—

R.C. 2,050,000 per c.cm.
W.C. 3,000 ,,
Hgb. Index 20 per cent.

Before death, which occurred early in September, spleen retracted two fingers' breadth above umbilicus. *Leishmania* sp. found post-mortem in spleen in enormous numbers, and in lesser numbers in liver.

places. Populations under five, deaths and indices have been tabulated as follows:—

Table 1

Locality	Persons under 5. Census 1901	Deaths, 1899-1908	Endemic index
Malta	19,684	686	3·4
Gozo	2,256	58	2·5
Malta—			
Valletta	2,295	40	1·7
Floriana	559	4	0·7
Senglea	914	10	1·0
Cospicua	1,475	43	2.9
Vittoriosa	693	14	2·0
Calcara	128	17	13·2
Zabbas	720	24	3·3
Tarxien and Paola	576	40	6·9
Zeitun and Marsascirocco	908	55	6·0
Asciak	217	20	9·2
Luca	335	13	3·8
Gudia	117	6	5·1
Chircop	82	9	10·9
Micabiba	158	12	7·5
Safi	53	4	7·5
Zurrico	452	38	8·4
Crendi	192	17	8·8
Misida and Pieta	539	21	3·8
Sliema and St. Julians	1,415	39	2·7
Hamrun	1,394	40	2·7
Birchircara	1,057	49	4·6
Curmi	1,193	22	1·8
Zebbug	624	20	3·2
Siggieui	395	32	8·1
Balzan Lia and Attard	464	16	3·4
Naxaro	414	6	1·4
Gargur	170	1	0·5
Musta	635	29	4·5
Imgiar and St. Paul's Bay	117	5	4·2
Melleha	372	2	0·5
Rabato and Dingli	1,007	36	3·5

Reference to Table 1 will show that the disease prevails in Malta more than in Gozo, and that the rural population, on the whole, is more heavily affected than the urban, the east of the Island more than the west, with an intermediate zone exhibiting intermediate intensity. Endemicity is lowest in Gargur, Melleha, Floriana and Senglea; Naxaro, Valletta and Curmi come next; whilst Calcara represents the highest. Zeitun, Tarxien, Asciak, Gudia, Safi, Micabiba, Chircop, Crendi and Zurrico, a group of villages to the

east of a line passing along the greater axis of the Island, and at no great distance one from the other, appear to suffer heavily, their indices varying from 6 to 10·9. One fact stands out: the low endemicity in the towns and the comparatively moderate endemicity in the suburban areas. To what extent this difference is attributable to certain conditions found to be more closely connected with our rural populations it would be rash to say at present. But the disease is such that less personal and domestic cleanliness, worse housing conditions, more frequent excremental pollution of soil and water, closer and more indiscriminate contact with domestic animals may very well help to spread.

Analysis of deaths, besides showing the prevalence of the disease to vary in the different populated centres, furnishes data for stating that the influence of locality is still more selective. Endemicity, in fact, is often found to be restricted to, or more intense in, some neighbourhoods or streets in preference to others. To a certain extent this may be accidental. But given the very protracted course of the disease, when the deaths do not happen to be separated by a lapse of several years, inference is justifiable that the specific virus has been conveyed from one house to the other by some common carrier. Allowing for changes of residence, which are not frequent in the villages, bringing together persons that were infected in different, and parting those that were infected in, the same streets, I believe the following graphs to be of interest. The broad lines represent roadways between blocks of buildings, the dots stand for houses from which deaths were registered, the figures in italics indicate the number of the houses, the others the year in which death occurred.

Age and sex. The total deaths under 5 for the period 1899-1908 were made up of 392 males and 352 females. Of 41 deaths at ages over 5, 16 were between 5 and 10 years of age.

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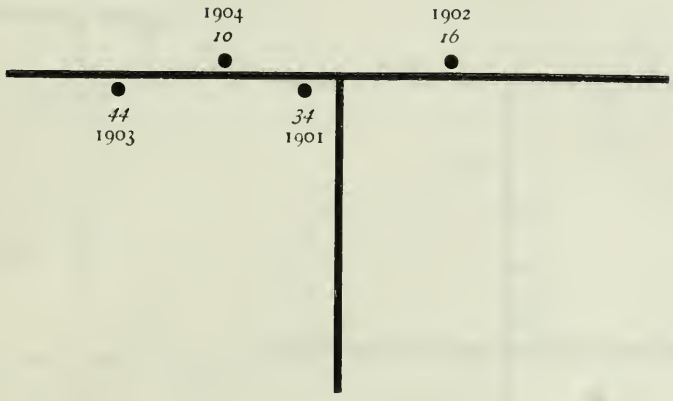
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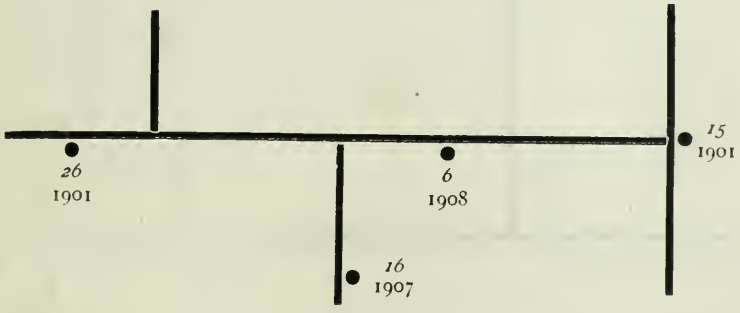
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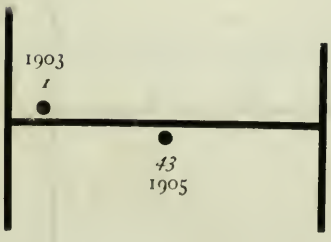
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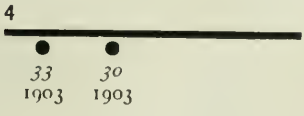
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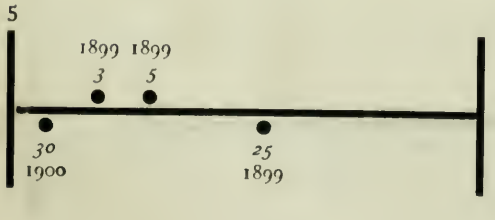
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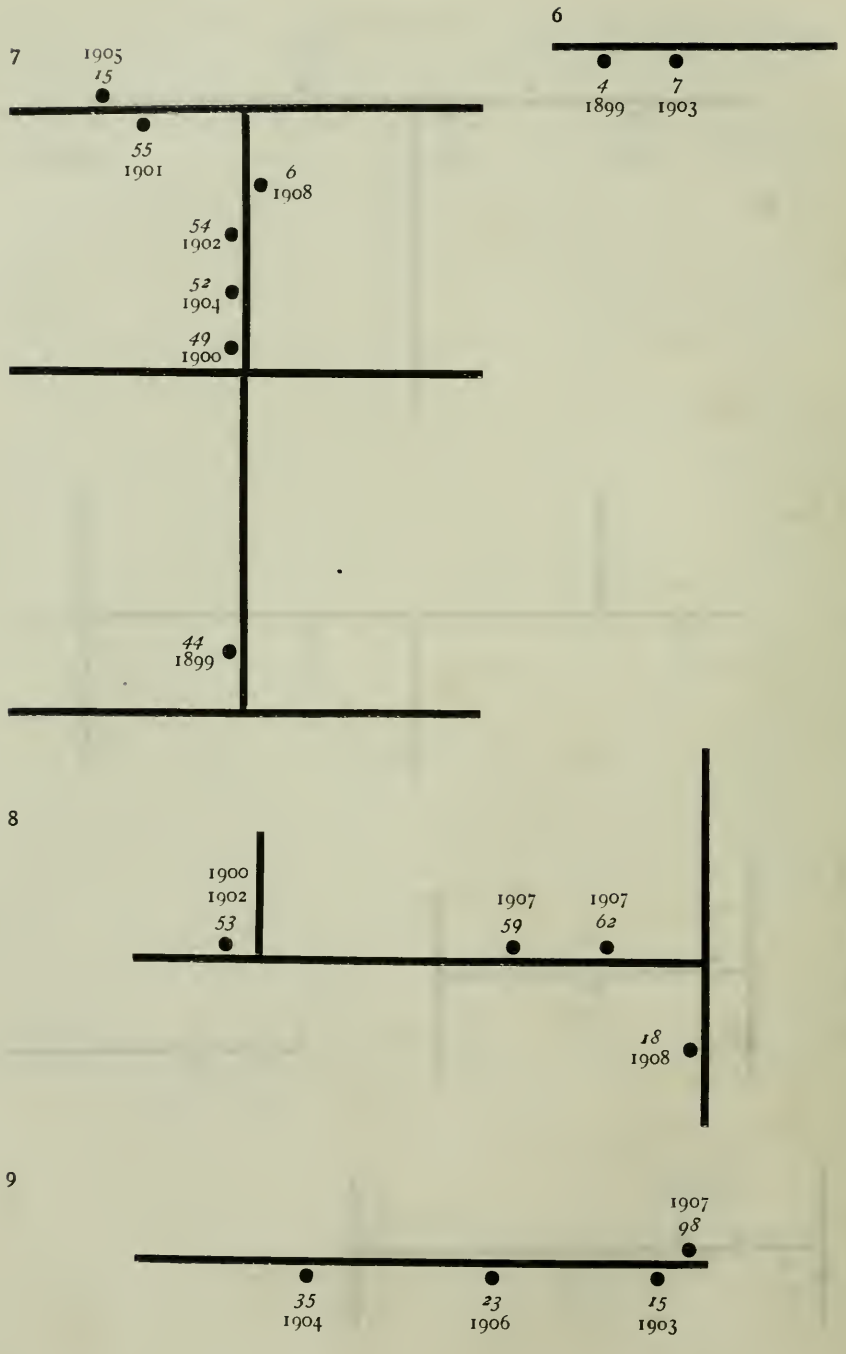
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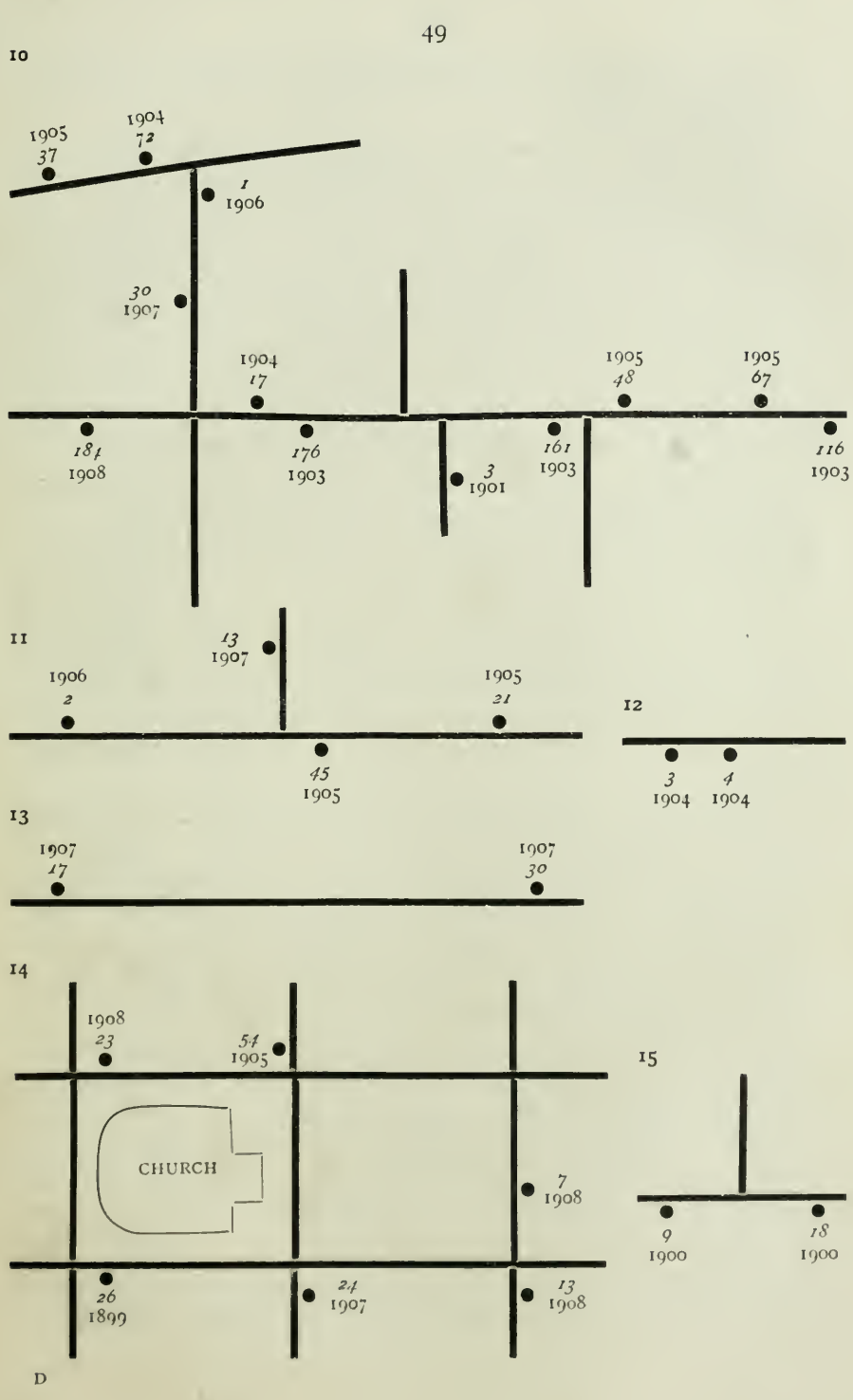
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In the succeeding table deaths have been grouped according to sex and age. (Table 2.)

Deaths under 1 appear to be equally distributed; but there is a distinct predominance of males over females at age group 1 to 2, which is responsible for nearly all the excess observed in the total males over females. Again, age-groups 1 to 2 contribute almost half the total deaths, 328, while the age-groups immediately preceding and following these account between them for 252 deaths. Owing to the protracted course of the disease, deaths recorded at ages below six months cannot be counted as caused by the disease unless it be assumed that this may prove fatal in a comparatively short time. As yet no such instances have been met with by me. Ponos, however, a disease endemic in the Greek islands of Spetsae and Hydra identical with 'marda tal biccia,' both as to its symptomatology and age of persons attacked, may prove fatal in one or two months.

Social circumstances are not specially restrictive of the disease, as cases do occur in families of well-to-do people, where the usual conditions associated with poverty are absent; its prevalence, however, appears to be more extensive among the children of the lower classes. Children born of English or Italian parents are not immune.

Recurrence of the disease in the same family and amongst relatives. Investigation has shown instances of brothers and sisters or first cousins dying of the disease to be not infrequent. Besides the cases that have come under my observation, I have been able to trace several others. These do not represent all that could be collected; but inquiry over a period reaching sometimes ten or twelve years back is for obvious reasons not easy, the more so when one has to overcome a not unnatural reticence founded on the belief that a sort of taint attaches to the disease. The view maintained by some practitioners that 'marda tal biccia' is a hereditary complaint is based on its aptitude to recur in two or more members of the same family. This standpoint is untenable both as regards direct transmission or transmission of proclivity if the following facts be duly considered, viz.: the special age incidence, the almost inexorably fatal termination of the disease, the healthiness of parents whose children are attacked, and of the

TABLE 2.—Showing for the Island of Malta the number of deaths from leucocythaemia, splenic leukaemia, splenic anaemia, pseudoleukaemia, splenitis, splenopathy under 5 and in several age groups in both sexes for the period 1899-1908, also number of deaths similarly certified during the same period for the Island of Gozo.

Locality	Sex	Age Groups									
		Under 3 months	3 months	6 months	Under 1 year	1 year	2 years	3 years	4 years	Under 5 years	Over 5 years
Malta	Males	9	12	58	80	182	76	21	9	368	—
	Females	8	11	50	70	146	68	29	5	318	—
	Total	17	23	108	150	328	144	50	14	686	41
Gozo	Males	—	—	—	—	—	—	—	—	24	?
	Females	—	—	—	—	—	—	—	—	34	?
	Total	—	—	—	—	—	—	—	—	58	?

brothers and sisters of the children attacked who very often are members of a large family.

Instances of recurrence in the same family and amongst cousins are here appended, showing sex, age at death, year and month in which they died. (Table 3.)

In Groups 1 to 12 and 18 the patient died before his or her sister or brother were born, in some cases several months intervening between the two events. The disease, therefore, cannot have been transmitted by direct contact. As it happens, belief in the communicability of 'marda tal biccia' is so rooted in the mind of the people that all articles of clothing and bedding used by the little patients are destroyed. Transmission by fomites is thus hindered to a considerable extent. Hence the existence of an intermediate parasite host becomes extremely probable. The sphere of action of an animal host would extend to members of different families in so far as their connections are more intimate and frequent. Generally speaking this is true of persons related by marriage and of their children. Instances of the disease among first cousins can thus be accounted for.

The specific cause of 'marda tal biccia' is a protozoon of the genus *Leishmania*. The parasites are morphologically identical with *Leishmania donovani*. Described first by G. Pianese, in 1905, in the splenic tissue from some cases of infantile splenic anaemia, they were observed in three cases of infantile splenomegaly in Tunis by C. Nicolle and E. Cassuto, in 1908, of which the former succeeded in cultivating the parasite and named it *Leishmania infantum*. Since then many similar observations have been made by Gabbi, Basile, Jemma, and Feletti in Southern Italy and Sicily; Sluka in Vienna; the writer in Malta*; Alvarez in Lisbon. Infantile leishmaniasis is found to have a daily widening endemicity. In common with other observers, the writer has found the Leishman bodies in the spleen, liver, kidneys and mesenteric glands, and once in films of peripheral blood. As the morphology and staining reactions of the parasite are well known, any mention here would be superfluous. Splenic puncture *intra vitam* was performed in

* Kala Azar Infantile à Malte. Note préliminaire. Archives de l'Institut Pasteur de Tunis. II. 1910.

TABLE 3—BROTHERS AND SISTERS

	Sex, and age at death	Year and month of death	Residence at time of death
1.	P.P., 2, male	Died March, 1904	Same house
	M.P., 6/12, female	,, November, 1904	
2.	R.C., 1 8/12, female	,, May, 1904	,,
	A.C., 1 1/12, male	,, July, 1905	
3.	E.P., 1 9/12, female	,, September, 1903	,,
	F.P., 10/12, female	,, January, 1907	
4.	L.M., 3, male	,, March, 1903	Different houses
	N.M., 1 4/12, male	,, March, 1906	
5.	C.C., 3, female	,, April, 1903	,,
	A.C., 2, male	,, August, 1907	
6.	C.V., 1½, female	,, August, 1901	Same house
	A.V., 1 3 12, female	,, November, 1907	
7.	C.G., 1, male	,, October, 1902	,,
	N.G., 1, female	,, February, 1905	
8.	A.P., 2½, male	,, March, 1902	,,
	C.P., 1½, male	,, April, 1904	
9.	A.X., 1 8/12, male	,, January, 1903	,,
	E.X., 1½, male	,, December, 1908	
10.	N.A., 2½, male	,, December, 1899	,,
	N.A., 2 4/12, male	,, May, 1904	
11.	M.C., 3, female	,, June, 1900	,,
	R.C., 2 1/12, female	,, November, 1902	
12.	L.D., 2, male	,, October, 1906	,,
	S.D., 1, female	,, May, 1908	
13.	G.A., 2 3/12, male	,, June, 1900	Same street, different number
	C.A., 1 2/12, male	,, July, 1901	
	R.A., 1½, female	,, October, 1903	
14.	P.C., 2 2/12, male	,, May, 1904	,,
	S.C., 4, female	,, November, 1907	
	M.C., 9/12, female	,, April, 1908	
15.	P.M., 3½, male	,, October, 1902	,,
	C.M., 2½, female	,, April, 1904	
16.	A.M., 3, male	,, July, 1907	Same house
	C.M., 1 10/12, male	,, December, 1907	
17.	M.F., 1½, female	,, October, 1901	,,
	G.F., 1, male	,, February, 1902	
18.	A.C., 1 7/12, female	,, March, 1904	,,
	R.C., 1 4/12, female	,, March, 1908	
19.	C.B., 1 8/12, female	,, September, 1899	,,
	G.B., 3, female	,, June, 1902	
20.	S.S., 3, male	,, November, 1904	,,
	E.S., 2, female	,, May, 1905	

Table 3—continued.—First Cousins

Sex and age at death	Year and month of death	Residence at time of death
21. S.B., 1 8/12, male	Died February, 1908	Different houses
S.B., 5, male	,, September, 1908	
22. C.M., 1½, female	,, January, 1902	,,
G.M.M., 2, male	,, July, 1907	
23. C.F., 1 10/12, female ... ... (Cousin to No. 4)	,, October, 1908	,,
24. A.C., 6½, male	,, May, 1903	Same street,
N.C., 1 7 12, male	,, February, 1903	different number
A.C., 1 4/12, male	,, December, 1903	Different street
25. A.G., 3, male ... ... (Cousin to No. 5)	,, February, 1908	Different houses
26. C.V.,10/12, female ... ... (Cousin to No. 6)	,, May, 1905	,,

five cases*: no untoward results were observed. The examination of the contents of blisters raised by vessication resorted to in two clinically typical cases of the disease proved negative. In several cases material for examination was available twenty-four hours or more after death, but the appearance of the Leishman bodies was still characteristic, only they were a little smaller than those obtained during life and their cytoplasm stained badly or not at all. The best specimens are obtained by splenic puncture *intra vitam*. The free parasites in the same film vary somewhat in size and shape, elongated and round forms are met with side by side; some have typical chromatin masses, in others the blepharoplast is punctiform, others, again, show the nucleus only. Forms are also met with containing two large chromatin masses, or nuclei, with or without a blepharoplast.

The writer found 7 out of 53 stray dogs examined post mortem in April and May, 1910, infected with *Leishmania*, sp.; 11 dogs seen in September were free. Some dogs were heavily infected, others less so, the parasites being always more numerous in the spleen than in the liver. The bone marrow was not examined. Almost all the

* In March, 1911, another case—a boy, 2 years—was diagnosed by splenic puncture.

infected dogs were small mongrels, some were mangy and extremely emaciated, one had chronic sores on the ischia and suppuration of the conjunctivae. A few ticks, of which some were gravid females off an infected dog, were dissected and examined with negative result.

Only in a few instances dogs have been found associated with human leishmaniasis, on the whole less frequently than expected. Until it be known how the virus is eliminated from the body of a naturally infected dog, and whether it may be withdrawn from its blood by blood-sucking insects, the results of my enquiries in this direction cannot minimise the importance of this animal as a probable factor in the transmission of the disease. If the excreta of an infected dog are able to carry infection or represent the means by which the parasite is dispersed about in order to undergo some as yet unknown developmental cycle, the presence of a diseased dog in a given street or neighbourhood is sufficient to explain the endemicity of 'marda tal biccia' in such street or neighbourhood.

In the light of this hypothesis the special incidence of the disease at certain ages below five, and its preference for the children of the lower classes are easy to explain.

By far the largest number of deaths occur between the 12th and 24th month of life, the next heaviest mortality is registered at ages between 24 and 36 months, the next again between the 6th and 12th months. It is not inconsistent with the variable duration of the disease for infection to occur when the child, having manifested more or less precociously a certain desire or ability to use its limbs, is put down to crawl. As long as the child is unable to do so the chances of infection appear to be very small. The families of the poorer classes, as a rule, live in the ground-floor, in the front room by preference, where they get more light and air; more often than not they have no other accommodation. The children crawl about through the doorway to the street. This ground they hold in common with the dog, that trots from door to door at its leisure. If the dog is a reservoir of the virus, its habits and the habits of children are so fitted that infection by ingestion or through skin abrasions is bound to occur.

The scope of this paper is to put on record that 'marda tal biccia' and anaemia infantum a leishmania, or infantile kala azar, are

one and the same disease, and to contribute to the study of some of the conditions associated with it.

As a specific parasitic complaint 'marda tal biccia' becomes *ipso facto* preventable.

The ease with which dogs contract experimental leishmaniosis, and the presence of infected dogs wherever infantile leishmaniosis has been shown to exist, make it extremely probable that the dog is a very important factor in the propagation and continued existence of the disease. The exact way of transmission is occupying the attention of several observers. Whether the dog be the only channel of infection, with or without the mediation of insects, or whether the disease be also contracted by one human being from another without the intervention of a lower animal, it is hoped that the epidemiology of the disease may be soon cleared up so that prophylactic measures may be applied on sound scientific lines.